REMARKS

I. Status of the Claims

Claims 75, 76, 78, 80, 82, 83, 88, 89, 91-106, and 108-112 were pending at the time the final Office Action dated May 11, 2010 ("the Action"), was mailed. Claims 75, 78, and 82 are independent claims that have been amended to narrow the scope of the claimed compounds. Claims 88, 91, 92, 93, 96, 97, 99, 100, and 101 are amended to reflect amendments made to Claims 75, 78, and 82. In particular, applicants note that support for amended Claim 91 appears at, e.g., page 15, lines 8-11, of the originally-filed specification, and support for amended Claim 99 may be found at page 13, lines 27-28, and page 15, lines 11-13. Claim 98 is amended to simply clarify the attachment points of the recited pyridinyl moiety.

Claim 92 is amended to restrict this claim to substituted aryl groups that are not further substituted. Amended Claim 93 is now drawn to particular substituted aryl groups that are not further substituted. New dependent Claim 113 recites substituted aryl groups omitted from amended Claim 92, but does not recite that these groups may be further substituted. New dependent Claim 114 recites a compound of formula (II) with A_1, A_2, R_1, R_2, and R_4 groups. No new matter is added by the amendments or by the new claims. Claims 104-106 are canceled. As such, Claims 75, 76, 78, 80, 82, 83, 88, 89, 91-103, and 108-114 are pending.

II. The Enablement Rejection Is Overcome

Claims 75, 76, 78, 80, 82, 83, 88, 89, 91-106, and 108-112 remain rejected under 35 U.S.C. § 112, first paragraph, as failing the enablement requirement. In particular, the Examiner contends that the genus of compounds is too broad, such as with respect to the A_2 variable. The Examiner also argues that the claims are not enabled because the specification fails to provide evidence that the compounds actually inhibit Raf kinase activity in a human or mammal. Because the compounds have "different functional groups" that result in "different

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biological properties," the claimed methods cannot be executed without undue experimentation, according to the Examiner. Action, page 6.

Applicants respectfully disagree. However, in an effort to advance prosecution and secure prompt allowance in this case, the scope of the compound genus in each claim has been narrowed. In particular, substituent A_1 now recites substituted aryl; A_2 now recites unsubstituted heteroaryl; R_1 and R_2 are now taken together to form a substituted heteroaryl; R_3 is hydrogen; and R_4 is hydrogen. In combination with applicants' previous amendment regarding Y, where Y is now only oxygen, applicants submit that the amended claims are enabled.

If the Examiner continues to disagree with the claim scope of the independent claims regarding the compound genus, applicants note the following dependent claims: Claims 91-95 and 113 further define A_1; Claims 96-98 further define A_2; Claims 99-103 further define R_1 and R_2; and Claims 88 and 89 further define R_4. Further, new Claim 114 defines a compound having narrower recitations of A_1, A_2, R_1, R_2, R_3, and R_4.

Turning to evidence of compounds actually inhibiting Raf kinase activity in a human or animal, applicants reiterate the arguments presented in the Response dated January 11, 2010, on this point, particularly with respect to the fact that breadth of structural diversity does not necessarily equal unpredictability. Although applicants do agree that as between two compounds having different A_1, A_2, R_1/R_2, and R_4 groups, those two compounds may have different activities, such a difference does not amount to a legal showing of the failure of the enablement requirement. This is especially true in light of the fact that compounds of Examples 1-1054 exhibit an IC_{50} with respect to Raf kinase activity of less than 5 μm. Specification, page 309, lines 14-15.

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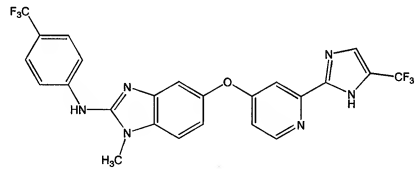
Applicants also respectfully reiterate the comments presented in the Response dated July 30, 2009, wherein applicants noted the *in vivo* data pertaining to a compound discussed in U.S. Patent No. 7,482,367 ("the '367 compound'):



This compound was shown to cause significant tumor growth inhibition or tumor regression in mice xenograft models of melanoma, colorectal carcinoma, and leukemia tumors. The '367 compound falls within the compound genus of the presently amended claims and shows substantial structural similarity to the claimed genus. Applicants submit that this *in vivo* evidence further demonstrates that the claims are enabled.

In view of the foregoing, applicants respectfully request that the enablement rejection be withdrawn.

III. The Double Patenting Rejection Is Overcome

Claims 75, 76, 78, 80, 82, 83, 88, 89, 91-106, and 108-112 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 43-45 of U.S. Application No. 12/315,779 ("the '779 application"). Applicants note that the '779 application has issued into U.S. Patent No. 7,732,465 ("the '465 patent"). Without conceding the propriety of the rejection, applicants submit a Terminal Disclaimer over the '465 patent. Withdrawal of the rejection is respectfully requested.

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CONCLUSION

In view of the foregoing, it is respectfully submitted that each of the pending claims is in condition for allowance, and a Notice of Allowance is requested. If any issues remain that may be expeditiously addressed in a telephone interview, the Examiner is encouraged to telephone applicants' attorney at 206.695.1649.

Respectfully submitted,

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